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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 10/538,716 | 06/10/2005 | Toshiya Fujisato | AKA-0286 | 6913 |

23599 7590 01/29/2007

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| EXAMINER | |
|---|---|
| MAKAR, KIMBERLY A | |
| ART UNIT | PAPER NUMBER |
| 1636 | |

| SHORTENED STATUTORY PERIOD OF RESPONSE | MAIL DATE | DELIVERY MODE |
|---|---|---|
| 3 MONTHS | 01/29/2007 | PAPER |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/538,716 | FUJISATO ET AL. | |
| | Examiner | Art Unit | |
| | Kimberly A. Makar | 1636 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *30 October 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1,2 and 4-10* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2 and 4-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *10 June 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

1. Applicant's amendments to claims and arguments entered on 10/30/06 are acknowledged. Cancellation of claim 3 by Applicant on 10/30/06 is acknowledged. Addition of claim 10 to the claim set is acknowledged. Currently, claims 1-2, 4-10 are pending.

2. Response to applicant's arguments are forthcoming in this action.

3. The following rejections were necessitated by Applicant's amendment entered on 10/30/06.

### *Claim Objections*

4. Claims 1 and 10 are objected to because of the following informalities: claims 1 and 10 misspell the word "de-cellularizing" as "de-cellularing".

5. Also, claims 1, 2 and 10 use both a hyphen, and non-hyphenated form of the word de-cellularizing (and their derivatives) seemingly indiscriminately. It would be remedial to chose one form and maintain consistency. Appropriate correction is required.

### *Claim Rejections - 35 USC § 112*

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1-2, 4-9 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

8. The specification as originally filed does not provide support for the invention as now claimed which recites a method of de-cellularizing native tissue of mammalian origin comprising directly and completely immersing said tissue in a treating solution, and irradiating the tissue with microwaves while maintaining the temperature of the tissue in the range of between 0°C and 40°C, and preventing tissue matrix from denaturing for a period of time to substantially de-cellularize said tissue. The specification does not provide sufficient blazemarks nor direction for the instant limitation of "directly" encompassed by the above-mentioned claim, as currently recited. The specification does not teach a limitation that the tissue is "directly" immersed. The specification does not teach the term "directly" nor in what circumstances "directly" is applied to the method. The instant claims now recite a limitation, which was not clearly disclosed in the specification as filed, and now changes the scope of the instant disclosure as filed. Such a limitation recited in the present claims, which did not appear in the specification as filed, introduces new concepts and violates the description requirement of the first paragraph of 35 U.S.C. 112..

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 1-2, 4-9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 1 recites the phrase "directly" in reference to the immersion of a tissue specimen in a treating solution in a method of de-cellularizing said tissue. The specification does not teach a limitation that the tissue is "directly" immersed. The specification does not teach the term "directly" nor in what circumstances "directly" is applied to the method. Does this refer to the handling of the tissue, in terms of the tissue being "directly" taken from the native source and immediately immersed in treating solution? What if the tissue has been cryopreserved? Does this refer to the tissue block being in direct contact with the immersion fluid, that there are no boundaries between the tissue and the immersion fluid? A skilled artisan would be unable to determine the metes and bounds of the claimed invention.

11. Claim 1 further recites the phrase, "a period of time to substantially de-cellullarize said tissue," which is unclear. It would seem that different tissues would require different amounts of time, depending up what type of tissue, and the size. While the specification and claims teach that the period of time ranges from 1 hour to 1 week, there are no guidelines on how long to perform the technique, in light of how de-cellularized the tissue becomes. What if there are 50% fewer cells? Thus 50% of the cells still remain. Is that long enough? What is there are 40% fewer? 30%? 20%? 10%? 5%? 1%? Etc. Without a teaching from the specification on how long to perform the method, or how to determine the "period of time" when dependent upon an

undisclosed limitation of "substantially decellularize[d]" a skilled artisan would be unable to determine the metes and bounds of the claimed invention.

***Claim Rejections - 35 USC § 102***

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

13. Claim 10 is rejected under 35 U.S.C. 102(b) as being anticipated by Anderson et al (US Patent No. 5,571,216). Claim 10 recites a method of de-cellularizing native tissue of mammalian origin comprising immersing said tissue in a treating solution, and irradiating the tissue with microwaves while maintaining the temperature of the tissue in the range between 0°C and 40°C, whereby said tissue is decellularized.

14. Anderson et al (US Patent No. 5,571,216) teaches a method of tissue welding comprising immersing the tissue in a welding bath (treating solution) and heating the tissue using a microwave (column 6, lines 1-6) at a temperature of 40°C (Column 8, line 37). Anderson specifically teaches mammalian tissue welding on bovine and porcine tissue (column 8, lines 28-43) as well as rabbit tendons and skin (column 9, lines 26-28). Anderson teaches that the welding bath comprises water (column 5, line 30). Anderson teaches that the native tissue to be treated includes vascular vessels as well as parts of whole organs including the gut (Column 1, lines 42-45). Finally, Anderson

teaches that the method of treatment further comprises quenching step (i.e. a washing step following irradiation) (column 8, lines 40-41). Thus Anderson teaches the claimed invention.

15. Claims 1-2, 4-9 are rejected under 35 U.S.C. 102(b) as being anticipated by Anderson et al (US Patent No. 5,571,216). This rejection is maintained for reasons of record in the previous Office Action (mailed 07/28/06) and for reasons outlined below.

16. Applicants have responded to this rejection by amending Claim 1 to recite that the method of "treating" a native tissue to a method of de-cellularizing a tissue comprising that the tissue is "directly and completely" immersed in a treating solution, microwaving the tissue, while maintaining the temperature range between 0°C and 40°C, and preventing tissue matrix from denaturing for a period of time to substantially decellularize the tissue. Applicant also argue, "[t]hus, it is apparent that the target to be heated is the contact area between the first and second materials, not the overall material." (page 4, response, dated 10/30/06). That, "[w]ater is not used as a bath in which tissue materials are immersed; the entirety of the material is not heated in the patent." And "[a]lthough Anderson refers to microwave heating (column 6, line 2), it does not disclose how the two materials are heated exclusively at the contact area between them using the microwave heating, particularly heating the tissue material in a water b[a]th." (page 5, response, dated 10/30/06). The claims as amended still read on the teaching of Anderson et al.

17. While the amendment changes the name of the method from "treatment" to de-cellularizing, the steps remain the same. Thus since Anderson teaches the steps, he

also therefore teaches a method of de-cellularizing. Secondly, the amendment "directly and completely" is not defined the in the instant application. Applicants do state that the whole tissue is immersed "completely" in the treatment solution (page 8, lines 2-4.) Using the broadest reasonable interpretation, the phrase "directly and completely" is being interpreted as the tissue specimen is immersed in the treatment solution completely, after "directly" being isolated from the donor (i.e. fresh tissue samples are being used.) Anderson teaches that the method comprises using fresh bovine and porcine tissue samples which are completely immersed in a water bath (i.e. "directly and completely" immersed.) Anderson also teaches that the period of timing for the method is important, and that the tissue is uniformly heated (column 4, lines 48-52.) Anderson further teaches that the method does not denature surrounding tissue after heating (column 8 line 57 through column 9, line 5.) Anderson teaches that the heating of the tissue occurs via microwaves (column 3, lines 10-13.) The examples of Anderson teach the immersion of the fresh samples are clamped together between sealed microscope coverslides and immersed in a water bath, which is heated, which results in welding. It is "after removal from the welding bath" that that samples are then tested for tensile strength (column 8, lines 28-42, particularly line 40). Thus Anderson teaches the claimed invention.

18. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP

§ 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kimberly A. Makar, Ph.D. whose telephone number is 571-272-4139. The examiner can normally be reached on 8AM - 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel, Ph.D. can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

kam/01/11/07

DAVID GUZO
PRIMARY EXAMINER